

PATENT

Appl. No. 09/322,219
Amend. dated August 24, 2004
Reply to Office Action of October 16, 2003. A Notice of
Appeal was filed April 14, 2004.

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings of claims in the application:

Listing of Claims:

1. (Currently Amended) A method of preventing or treating a disease characterized by an amyloid deposit comprising A β peptide in a patient, the method comprising administering to the a patient having the disease an antibody that specifically binds to A β peptide, in a regime effective to prevent or treat the disease, wherein the administering of the antibody reduces levels of A β in the brain of the patient wherein the antibody is a chimeric or humanized antibody, or a human monoclonal antibody and the antibody is of isotype human IgG1.

2. (Original) The method of claim 1, wherein the disease is Alzheimer's disease.

3. (Canceled)

4. (Original) The method of claim 1, wherein the patient is a human.

5. (Canceled)

6. (Original) The method of claim 1, wherein the patient is under 50.

7. (Original) The method of claim 1, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.

8. (Original) The method of claim 1, wherein the patient has no known risk factors for Alzheimer's disease.

9. (Canceled)

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10. (Currently Amended) The method of claim 2, wherein the antibody is a human monoclonal antibody.
11. (Previously Presented) The method of claim 2, wherein the antibody is a humanized antibody.
12. (Previously Presented) The method of claim 2, wherein the antibody is a chimeric antibody.
13. (Canceled)
14. (Previously Presented) The method of claim 2, wherein the antibody is a polyclonal antibody.
15. (Previously Presented) The method of claim 2, wherein the antibody is a monoclonal antibody.
16. (Canceled)
17. (Original) The method of claim 1, further comprising administering an effective dosage of a second antibody that binds to the amyloid deposit or a component thereof.
- 18-20. (Canceled)
21. (Previously Presented) The method of claim 2, wherein a chain of the antibody is fused to a heterologous polypeptide.
22. (Previously Presented) The method of claim 2, wherein the dosage of antibody is at least 1 mg/kg body weight of the patient.
23. (Previously Presented) The method of claim 2, wherein the dosage of antibody is at least 10 mg/kg body weight of the patient.

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24. (Previously Presented) The method of claim 2, wherein the antibody is administered with a carrier as a pharmaceutical composition.

25. (Withdrawn) The method of claim 9, wherein the antibody binds to an epitope within residues 1-28 of A β .

26. (Withdrawn) The method of claim 25, wherein the antibody binds to an epitope within residues 1-10 of A β .

27. (Withdrawn) The method of claim 25, wherein the antibody binds to an epitope within residues 1-16 of A β .

28. (Withdrawn) The method of claim 25, wherein the antibody binds to an epitope within residues 1-5 of A β .

29-30. (Canceled)

31. (Previously Presented) The method of claim 2, wherein the antibody specifically binds to A β peptide without binding to full-length amyloid precursor protein (APP).

32. (Previously Presented) The method of claim 1, wherein the antibody is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.

33. (Withdrawn) The method of claim 1, wherein the antibody is administered by administering a polynucleotide encoding at least one antibody chain to the patient, wherein the polynucleotide is expressed to produce the antibody chain in the patient.

34. (Withdrawn) The method of claim 33, wherein the polynucleotide encodes heavy and light chains of the antibody, which polynucleotide is expressed to produce the heavy and light chains in the patient.

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35. (Original) The method of claim 1, further comprising monitoring the patient for level of administered antibody in the blood of the patient.

36. (Original) The method of claim 1, wherein the antibody is administered in multiple dosages over a period of at least six months.

37. (Original) The method of claim 1, wherein the antibody is administered as a sustained release composition.

38. (Withdrawn) A method of preventing or treating Alzheimer's disease, comprising administering an effective dosage of a polypeptide comprising an active fragment of A β that induces an immune response to A β in the patient.

39. (Withdrawn) The method of claim 38, wherein the fragment comprises an epitope within amino acids 1-12 of A β .

40. (Withdrawn) The method of claim 38, wherein the fragment comprises an epitope within amino acids 1-16 of A β .

41. (Withdrawn) The method of claim 38, wherein the fragment comprises an epitope within amino acids 13-28 of A β .

42. (Withdrawn) The method of claim 38, wherein the fragment is free of at least the 5 C-terminal amino acids in A β 43.

43. (Withdrawn) The method of claim 38, wherein the fragment comprises up to 20 contiguous amino acids from A β .

44. (Withdrawn) The method of claim 39, wherein the fragment is administered with an adjuvant that enhances the immune response to the A β peptide.

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45. (Withdrawn) The method of claim 44, wherein the adjuvant and the agent are administered together as a composition.

46. (Withdrawn) The method of claim 44, wherein the adjuvant is administered before the agent.

47. (Withdrawn) The method of claim 44, wherein the adjuvant is administered after the agent.

48. (Withdrawn) The method of claim 44, wherein the adjuvant is alum.

49. (Withdrawn) The method of claim 44, wherein the adjuvant is MPL.

50. (Withdrawn) The method of claim 44, wherein the adjuvant is QS-21.

51. (Withdrawn) The method of claim 44, wherein the adjuvant is incomplete Freund's adjuvant.

52. (Withdrawn) The method of claim 44, wherein the dosage of the fragment is greater than 10 micrograms.

53. (Withdrawn) A pharmaceutical composition comprising an active fragment of A β effective to induce a response to AB in a patient and an adjuvant.

54. (Withdrawn) A method of screening an antibody to A β or an active fragment of A β for use in treatment of Alzheimer's disease, comprising:

administering an antibody that specifically binds to A β or a fragment of AB to a transgenic animal disposed to develop characteristics of Alzheimer's disease;

detecting a reduction in the extent or rate of development of the characteristics relative to a control transgenic animal.

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55. (Withdrawn) The method of claim 54, further comprising screening a population of antibodies to identify an antibody that binds to an epitope within amino acids 1-28 of A β .

56. (Withdrawn) The method of claim 1, wherein the antibody is administered at a site separated by the blood-brain barrier from the brain.

57. (Withdrawn) The method of claim 1, wherein the antibody specifically binds to A β in disaggregated form with a binding affinity of at least $10^7 M^{-1}$.

58. (Withdrawn) The method of claim 56, wherein the antibody specifically binds to A β 41.

59. (Canceled)

60. (Withdrawn) The method of claim 1, wherein the administering of the antibody results in an amelioration of symptoms determined by a psychometric measure.

61. (Withdrawn) The method of claim 60, wherein the psychometric measure is a Mini-Mental State Examination score.

62. (Withdrawn) The method of claim 60, wherein the psychometric measure is an ADAS score.

63. (Withdrawn) The method of any one of claims 60-62, further comprising determining the psychometric measure.

64. (Withdrawn) The method of claim 1, further comprising monitoring progression of Alzheimer's disease in the patient using MRI.

65. (Withdrawn) The method of claim 35, further comprising administering an additional dosage of antibody responsive to a decrease in the measured level of antibody.

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66. (Withdrawn) The method of claim 1, wherein the antibody is a human antibody of IgG1 isotype.

67. (Withdrawn) The method of claim 58, wherein the antibody is administered with a carrier as a pharmaceutical composition to the patient.

68. (Withdrawn) The method of claim 1, wherein the antibody specifically binds to A β peptide in an amyloid deposit.

69. (Withdrawn) The method of claims 1 or 68, wherein the dosage of antibody is at least 1 mg/kg body weight of the patient.

70. (Withdrawn) The method of claim 1, wherein the antibody is administered on multiple occasions.

71. (Withdrawn) The method of claim 1, wherein the intervals between single dosages is once every week, once per every two weeks, once a month, once every 3 to 6 months, or yearly.

72. (Withdrawn) The method of claim 1, wherein the intervals are irregular as indicated by measuring blood levels of A β in the patient.

73. (Withdrawn) The method of claim 1, wherein administration of a further dosage of antibody is administered when the level of the antibody has declined to baseline measurement of the antibody in the patient before administration of the antibody.

74. (Withdrawn) A method of preventing or treating a disease characterized by amyloid deposit comprising A β peptide in a patient, comprising administering to the patient an antibody that specifically binds to A β peptide, in a regime effective to prevent or treat the disease, wherein the dosage of antibody is at least 1 mg/kg body weight of the patient.

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75. (Withdrawn) The method of claim 74, wherein the antibody specifically binds to A β in an amyloid deposit.

76. (Withdrawn) The method of claim 74 or 75, wherein the antibody is administered on multiple occasions.

77. (Withdrawn) The method of claim 76, wherein the intervals between single dosages is once every week, once per every two weeks, once a month, once every 3 to 6 months, or yearly.

78. (Withdrawn) The method of claim 76, wherein the intervals are irregular as indicated by measuring blood levels of A β in the patient.

79. (Withdrawn) The method of claim 76, wherein administration of a further dosage of antibody is administered when the level of the antibody has declined to baseline measurement of the antibody in the patient before administration of the antibody.

80. (Withdrawn) The method of claim 1, wherein the antibody is a human antibody or a humanized antibody, and the antibody binds an epitope within residues 1-10 of A β .

81. (Withdrawn) The method of claim 74, wherein the antibody is a human antibody or a humanized antibody, and the antibody binds an epitope within residues 1-10 of A β .

82. (New) A method of prophylaxis of a disease characterized by an amyloid deposit comprising A β peptide, comprising administering to a patient an antibody that specifically binds to A β peptide, in a regime effective to effect prophylaxis of the disease, wherein the antibody is a chimeric or humanized antibody, or a human monoclonal antibody, and the antibody is of isotype human IgG1.

83. (New) The method of claim 82, wherein the disease is Alzheimer's disease.

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84. (New) The method of claim 82, wherein the patient is a human.
85. (New) The method of claim 82, wherein the patient is under 50.
86. (New) The method of claim 82, wherein the patient has inherited risk factors indicating susceptibility to Alzheimer's disease.
87. (New) The method of claim 82, wherein the patient has no known risk factors for Alzheimer's disease.
88. (New) The method of claim 82, wherein the antibody is the human monoclonal antibody.
89. (New) The method of claim 82, wherein the antibody is the humanized antibody.
90. (New) The method of claim 82, wherein the antibody is the chimeric antibody.
91. (New) The method of claim 82, wherein the antibody is a polyclonal antibody.
92. (New) The method of claim 82, wherein the antibody is a monoclonal antibody.
93. (New) The method of claim 82, further comprising administering an effective dosage of a second antibody that binds to the amyloid deposit or a component thereof.
94. (New) The method of claim 82, wherein a chain of the antibody is fused to a heterologous polypeptide.
95. (New) The method of claim 82, wherein the dosage of antibody is at least 1 mg/kg body weight of the patient.

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96. (New) The method of claim 82, wherein the dosage of antibody is at least 10 mg/kg body weight of the patient.

97. (New) The method of claim 82, wherein the antibody is administered with a carrier as a pharmaceutical composition.

98. (New) The method of claim 82, wherein the antibody specifically binds to A β peptide without binding to full-length amyloid precursor protein (APP).

99. (New) The method of claim 82, wherein the antibody is administered intraperitoneally, orally, subcutaneously, intramuscularly, topically or intravenously.

100. (New) The method of claim 82, further comprising monitoring the patient for level of administered antibody in the blood of the patient.

101. (New) The method of claim 82, wherein the antibody is administered in multiple dosages over a period of at least six months.

102. (New) The method of claim 82, wherein the antibody is administered as a sustained release composition.